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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/014,220	11/09/2001	Che-Kun James Shen	514162000120	5165

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MORRISON & FOERSTER LLP
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EXAMINER

KAUSHAL, SUMESH

ART UNIT PAPER NUMBER

1636

DATE MAILED: 05/03/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/014,220

Applicant(s)

SHEN, CHE-KUN JAMES

Examiner

Sumesh Kaushal Ph.D.

Art Unit

1636

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 19 January 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 21-34 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 21-34 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Applicant's response filed on 01/19/05 has been acknowledged.

Claims 1-20 are canceled.

Claims 21-34 are pending and are examined in this office action.

Applicants are required to follow Amendment Practice under revised 37 CFR §1.121. The fax phone numbers for the organization where this application or proceeding is assigned is 571-273-8300.

Terminal Disclaimer

The terminal disclaimer filed on 01/19/05 disclaiming the terminal portion of any patent granted on this application, which would extend beyond the expiration date of US 6,303,845 has been reviewed and is accepted. The terminal disclaimer has been recorded.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 21-34 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The scope of claim 21 encompasses an isolated animal cell and progeny thereof. Given the broadest reasonable interpretation the scope of invention as claimed encompasses a human embryonic cell wherein the progeny of the cell is a developed human being. It is PTO policy not to allow claims to

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humans (1077 O.G. 24 April 1987). The insertion of non-human before animal and progeny thereof, would overcome this rejection.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 21, 23-27 and 30-32 are rejected under 35 U.S.C. 102(b) as being anticipated by Zhang et al (JBC 270(15):8501-8505, 1995, *ref of record on PTO 1449*).

The scope of invention as claimed encompasses an isolated cell comprising a transcriptional start site a promoter operably linked to the start site and an enhancer operably linked to the promoter, wherein the enhancer comprises the nucleotide sequences of SEQ ID NO:1. The scope of invention as claimed further encompasses a cell wherein the promoter (ζ -globin promoter) drives the transcription of a polypeptide (growth hormone).

Zhang teaches that HS-40 consists of multiple nuclear factor binding motifs that are occupied *in-vivo* in an erythroid lineage and developmental stage-specific manner. The cited art further teaches systematically analysis and functional roles of these factor-binding motifs of HS-40 by site-directed mutagenesis and transient expression assay in erythroid cell cultures. The cited art teaches that three of these HS-40 enhancer motifs, 5'NF-E2/AP1, GT II, and GATA-1(c), positively regulate the ζ -globin promoter activity in embryonic/fetal erythroid K562 cells and the adult α -globin promoter activity in adult erythroid MEL cells. The cited art further teaches that on the other hand, the 3'NF-E2/AP1 motif is able to exert both positive and negative regulatory effects on the ζ -globin promoter activity in K562 cells, and this dual function appears to be modulated

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through differential binding of the ubiquitous AP1 factors and the erythroid-enriched NF-E2 factor (page 8561, abstract). The cited art further teaches an expression vector comprising, a tissue specific ζ -globin promoter operably linked to a HS-40 enhancer and a transcriptional start site that drives the expression of human growth hormone (page 8502 col.1 para.4; col.2 para 2-4). The cited art further teaches transfection of host cell using at least 10 μ g of plasmid construct that inherently incorporated 5-15 copies of transgene. The cited art further teaches a HS-40 enhancer element (NF-E2/AP1-II) which comprises the nucleotide sequence of SEQ ID NO:1 (**tctgagtca**) see page 8503, fig-1B, 3'NF-E2/AP1-II. The cited art further teaches a method of expressing p-HS40 (3'NF-E2/AP1-II)- ζ 597GH expression vector into isolated K562 erythroid cells. The genetically modified K562 cells were transfected with expression vector and the expression of growth hormone was measured by GH assay and/or RNA primer extension assay (page 8503 fig 1 and 2). The cited art further teaches that mutant HS-40 enhancer comprises a 1-bp mutation in the 3'NF-E2/AP1 motif (gctgagtca to **tctgagtca**) that exhibited a 2-3 fold higher level of enhancer activity than the wild type HS-40 enhancer (page 8502, col.2 para.6; page 8504 fig-3). Thus the cited art clearly anticipate the invention as claimed.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 22, 28-29 and 33-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zhang et al (JBC 270(15):8501-8505, 1995, *ref of record on PTO*

1449) as applied to claims 21-27 and 30-32 above, and further in view of Zhang et al (Mol Cell Biol. 4:2298-308, 1993, *ref of record on PTO 1449*).

Zhang (1995) is discussed detail above. Even though Zhang inherently teaches an expression vector comprising a 373 bp fragment of HS40 enhancer region, which contain a mutated HS-40 enhancer element (NF-E2/AP1-II) comprising the nucleotide sequence of SEQ ID NO:1 (**tctgagtca**), Zhang does not teach nucleic acid sequences comprising SEQ ID NO:2 and SEQ ID NO:3 of instant application.

Zhang 1993 teaches a nucleotide sequence for HS-40 enhancer element which matches to the nucleotide sequences of SEQ ID NO:2 and SEQ ID NO:3 (page 2299, fig-1B). The cited art specifically teaches mutated HS-40 enhancer element (NF-E2/AP1) which comprises the nucleotide sequence of SEQ ID NO:1 (page 2304, col.1 fig-7A). In addition the cited art teaches transcriptional activation of human embryonic zeta 2 globin gene and the fetal/adult alpha-globin gene is mediated by erythroid cell-specific and developmental stage-specific nuclear factor-DNA complexes, which form at the enhancer (HS-40) and the globin promoters. Furthermore in view of prior art that teaches genetic modification of human and Hela cells, the transfection of other animal cells is obvious if not anticipated in view of cited prior art of record

Thus it would have been obvious that genetically modified embryonic/fetal erythroid K562 and adult erythroid MEL cells as disclosed by Zhang (1995) inherently comprises an expression vector that contains a **tctgagtca** mutated cited in the HS40 enhancer element of Zhang (1993). Alternatively it would have been obvious to use the flanking regions around the **tctgagtca** element, since HS-40 consists of multiple nuclear factor binding motifs that are occupied *in-vivo* in an erythroid lineage and developmental stage-specific manner. One would have been motivated to include the flanking regions around the **tctgagtca** element in order to regulate erythroid developmental in a stage-specific fashion. One would have a reasonable expectation of success because the genetic modification of HS40 enhancer elements by site directed mutagenesis has been well known in the art at the time the instant invention was made. Thus the invention as claimed is prima facie obvious in view of cited prior art of record.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sumesh Kaushal Ph.D. whose telephone number is 571-272-0769. The examiner can normally be reached on Mon-Fri. from 9AM-5PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yucel Irem Ph.D. can be reached on 571-272-0781.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to **571-272-0547**. For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199. The fax phone number for the organization where this application or proceeding is assigned is **571-273-8300**.

Sumesh Kaushal
Examiner GAU 1636



SUMESH KAUSHAL
PATENT EXAMINER